

# ATTACHMENT 1

## Cholecystokinin

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**Cholecystokinin** (**CCK**; from Greek *chole*, "bile"; *cysto*, "sac"; *kinin*, "move"; hence, *move the bile-sac (gallbladder)*) is a peptide hormone of the gastrointestinal system responsible for stimulating the digestion of fat and protein. Cholecystokinin, previously called *pancreozymin*, is secreted by the duodenum, the first segment of the small intestine, and causes the release of digestive enzymes and bile from the pancreas and gallbladder, respectively. It also acts as a hunger suppressant. Recent evidence has suggested that it also plays a major role in inducing drug tolerance to opioids like morphine and heroin, and is partly implicated in experiences of pain hypersensitivity during opioid withdrawal..

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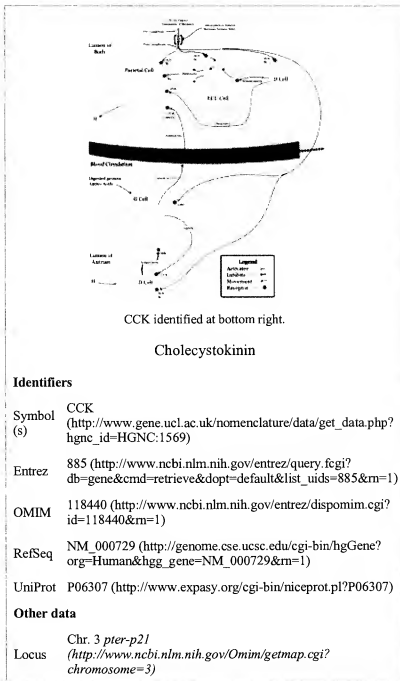
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### Structure

CCK is composed of varying numbers of amino acids (e.g., CCK58, CCK33, CCK8) depending on post-translational modification of the CCK gene product, preprocholecystokinin. CCK is very similar in structure to gastrin, another of the gastrointestinal hormones, so much so that the last five C-terminal amino acids are same as those of gastrin. CCK58 is comprised of a helix-turn-helix configuration.

### Function

CCK mediates a number of physiological processes, including digestion and satiety.



## Digestion

CCK is secreted by the duodenal mucosa when fat- or protein-rich chyme leaves the stomach and enters the duodenum. The hormone acts on the pancreas to stimulate the secretion of a juice rich in digestive enzymes, including trypsinogen, chymotrypsinogen (which are converted to trypsin and chymotrypsin in the duodenum), amylase and lipase. Together these pancreatic digestive enzymes catalyze the digestion of fat, protein, and carbohydrate.

CCK also causes the increased production of hepatic bile, and stimulates the contraction of the gallbladder and the relaxation of the Sphincter of Oddi (Glisson's sphincter), resulting in the delivery of bile into the duodenal part of the small intestine. Bile salts form amphipathic micelles that emulsify fats, aiding in their digestion and absorption.

## Neurobiology

As a neuropeptide, CCK mediates satiety by acting on the CCK receptors distributed widely throughout the central nervous system. In humans, CCK administration causes nausea and anxiety, and weakly decreases the desire to eat [1] ([http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list\\_uids=9855480&dopt=Abstract](http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=9855480&dopt=Abstract)).

The effects of CCK vary between individuals. For example, in rats, CCK administration significantly reduces hunger in young males, but is less effective in older subjects, and even less effective in females. The hunger-suppressive effects of CCK also diminish in obese rats [2] ([http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list\\_uids=9835394](http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=9835394)).

## References

- Greenough A, Cole G, Lewis J, Lockton A, Blundell J (1998). "Untangling the effects of hunger, anxiety, and nausea on energy intake during intravenous cholecystokinin octapeptide (CCK-8) infusion". *Physiol Behav* **65** (2): 303-10. PMID 9855480 ([http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list\\_uids=9855480](http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=9855480)).
- Fink H, Rex A, Voits M, Voigt JP (1998). "Major biological actions of CCK--a critical evaluation of research findings". *Exp Brain Res* **123** (1-2): 77-83. PMID 9835394 ([http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list\\_uids=9835394](http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=pubmed&dopt=Abstract&list_uids=9835394)).

## External links

- Cholecystokinin, NIH/NLM Medical Subject Headings (<http://www.nlm.nih.gov/cgi/mesh/2K/MB.cgi?term=Cholecystokinin>)

### Hormones and endocrine glands

**Hypothalamus**: - TRH - CRH - GnRH - GHRH - somatostatin - dopamine | **Posterior pituitary**: vasopressin - oxytocin - lipotropin | **Anterior pituitary**: GH - ACTH - TSH - LH - FSH - prolactin - MSH - endorphins - lipotropin

**Thyroid**: T<sub>3</sub> and T<sub>4</sub> - calcitonin | **Parathyroid**: PTH | **Adrenal medulla**: epinephrine - norepinephrine | **Adrenal cortex**: aldosterone - cortisol - DHEA | **Pancreas**: glucagon- insulin - somatostatin | **Ovary**: estradiol - progesterone - inhibin - activin | **Testis**: testosterone - AMH - inhibin | **Pineal gland**: melatonin | **Kidney**: renin - EPO - calcitriol - prostaglandin | **Heart atrium**: ANP

**Stomach**: gastrin | **Duodenum**: CCK - GIP - secretin - motilin - VIP | **Ileum**: enteroglucagon | **Liver**: IGF-1

**Placenta:** hCG - HPL - estrogen - progesterone

**Adipose tissue:** leptin, adiponectin

**Target-derived** NGF, BDNF, NT-3

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Categories: Hepatology | Intestinal hormones | Neuropeptides

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